REMARKS

The non-final Office Action dated August 19, 2008 ("Office Action") has been carefully considered.

Claims 1-42 are pending in this application. Claims 1, 3, 25, 27, 33-36 and 39-41 have been withdrawn by the Examiner as being drawn to non-elected inventions.

In the Office Action (see page 2, first paragraph), the Examiner alleges that the species election was made without traverse in the Amendment filed on April 9, 2008. Applicants respectfully disagree and wish to direct the Examiner's attention to Applicants' remarks on page 9 of the Amendment filed on April 9, 2008 and page 8 of the Response to Restriction Requirement and Preliminary Amendment filed on November 5, 2007, in which Applicants traversed the withdrawal of claim 1. Specifically, Applicants stated in these replies that claim 1 is generic, since the recitation in claim 1 of "a method of treating a puncture in a vein or artery" encompasses both the elected species claim 2, which is directed to "a method of treating a puncture in a femoral artery," and the non-elected species of claim 1, which is directed to "a method of treating a puncture in a vein." Applicants requested reconsideration of the withdrawal of claim 1 in the Amendment filed on April 9, 2008, and hereby again request reconsideration of the status of claim 1, especially in view of the fact that the Restriction Requirement dated July 5, 2007 indicates that claims 1 and 2 belong to the same group of invention, *i.e.*, Group I.

Claims 32-36 and 40 have been cancelled without prejudice. Applicants reserve the right to pursue the subject matter of the cancelled claims in this application or one or more related applications.

Claims 1-3 and 39 have been amended and new claims 43-46 have been added for purposes of clarity. Support for the amendments and new claims can be found in the specification as set forth in the chart below.

Claim(s)	Amendment	Support
1, 2	"a patient in need of such treatment"	**[0045]**
1, 2, 3, 39	"and concurrently applying compression"	**[0056]**
3	"a patient in need of such inhibition"	**[0034]**
39	"a patient at risk of said complications"	**[0026]**
39	"an effective amount"	**[0026]**
43-46	"the compression is applied for at least one time interval of up to ten minutes"	**[0056]**

In addition, claims 14, 19 and 22 have been amended to correct a few minor editorial errors. No new matter has been added.

Upon entry of the amendments made herein, claims 1-31, 37-39 and 41-46 will be pending in this application.

I. THE CLAIM REJECTIONS UNDER 35 U.S.C. § 102(b) SHOULD BE WITHDRAWN

Claims 2, 4-5, 7, 14, 15, 21, 22, 26, 28, 29, 31, 37 and 38 are rejected under 35 U.S.C. § 102(b) ("Section 102(b)") as allegedly being anticipated by U.S. Patent No. 5,437,292 to Kipshidze *et al.* ("Kipshidze"). Applicants respectfully disagree for the reasons set forth below.

A. Legal Standard

With respect to rejections of claims under 35 U.S.C. § 102(b), the Federal Circuit has affirmed that "an anticipating reference must describe and enable the claimed invention, including all the claim limitations, with sufficient clarity and detail to establish that the subject matter already existed in the prior art and that its existence was recognized by persons of ordinary skill in the field of the invention." *In re Spada*, 911 F.2d 705, 708, 15 U.S.P.Q.2d 1655, 1657 (Fed. Cir. 1990); *Crown Operations International, Ltd. v. Solutia Inc.*, 289 F.3d 1367, 1375, 62 U.S.P.Q.2d 1917, 1921 (Fed. Cir. 2002). The standard for an anticipatory reference is set forth in *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987): "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *See also Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 U.S.P.Q.2d 1913, 1920 (Fed. Cir. 1989) (holding that "[t]he identical invention must be shown in as complete detail as is contained in the...claim").

B. Kipshidze Does Not Anticipate Amended Claim 2 and Dependent Claims 4, 5, 7, 14, 15, 21, 22, 26, 28, 29, 31, 37 and 38

As a preliminary matter, independent claim 2 has been amended to clarify certain embodiments of the invention. As amended, claim 2 recites a method for treating a puncture in a femoral artery resulting from a cardiac catheterization procedure in a patient, comprising: a) applying topically over a catheter exit site on the skin of a patient in need of such treatment

a composition comprising an effective amount of one or more vasoconstrictor, wherein the vasoconstrictor does not comprise a poly-β-1→4N-acetylglucosamine polymer or derivative thereof, and wherein the catheter exit site is contiguous with the catheter puncture in the femoral artery by 1-10 cm; and concurrently b) applying compression to the punctured femoral artery. Claims 4, 5, 7, 14, 15, 21, 22, 26, 28, 29, 31, 37 and 38 depend on amended claim 2 and, therefore, include all the recitations of amended claim 2.

Kipshidze does not teach or suggest a method for treating a puncture in a femoral artery resulting from a cardiac catheterization procedure in a patient by applying topically over a catheter exit site on the skin of a patient in need of such treatment a composition comprising an effective amount of one or more vasoconstrictor which does not comprise a poly-β-1→4N-acetylglucosamine polymer or derivative thereof, as recited in amended claim 2. Instead, Kipshidze teaches administering a composition percutaneously, *i.e.*, via needle-puncture of the skin (see Abstract). Specifically, Kipshidze discloses introducing a fibrin sealant through the patient's skin, directly to the tissue adjacent to the vicinity of the puncture site in a blood vessel (see, *e.g.*, col. 5, lines 51-52 and see col. 2, line 49 to col. 3, line 21). Therefore, Kipshidze fails to teach each and every element of amended claim 2.

For at least the foregoing reasons, amended claim 2, and claims 4, 5, 7, 14, 15, 21, 22, 26, 28, 29, 31, 37 and 38, to the extent that they depend from claim 2, are not anticipated by Kipshidze. Withdrawal of the Section 102(b) rejection is respectfully requested.

II. THE CLAIM REJECTIONS UNDER 35 U.S.C. § 103(a) SHOULD BE WITHDRAWN

Claims 6, 19, 20, 23 and 42 are rejected under 35 U.S.C. § 103(a) ("Section 103(a)") as allegedly being obvious over Kipshidze in view of U.S. Patent No. 6,162,241 to Coury *et al.* ("Coury"). Claims 8-13, 16-18, 24 and 30 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Kipshidze in view of U.S. Patent Application Publication No. 2002/0197302 to Cochrum *et al.* ("Cochrum"). Claim 32 is rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Kipshidze. Applicants respectfully disagree for the reasons set forth below.

A. Legal Standard

In *KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 82 U.S.P.Q. 1385 (2007), the Supreme Court stated that the following factors set forth in *Graham v. John Deere Co.*,

383 U.S. 1, 148 U.S.P.Q. 459 (1966) still control an obviousness inquiry: (1) the scope and content of the prior art; (2) the differences between the prior art and the claimed invention; (3) the level of ordinary skill in the art; and (4) objective evidence of nonobviousness. *KSR*, 127 S.Ct. at 1734, 82 U.S.P.Q.2d at 1388 (quoting Graham, 383 U.S. at 17-18, 14 U.S.P.Q. at 467).

In order to establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580 (CCPA 1974). Additionally, the Supreme Court, in *KSR*, affirmed that "a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art," and that it is "important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does...because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known." *KSR*, S.Ct. at 1741, 82 U.S.P.Q.2d at 1396. Further, under *KSR*, "a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions." *KSR*, S.Ct. at 1740, 82 U.S.P.Q.2d at 1396. The relevant inquiry is whether the prior art suggests the invention and whether the prior art provides one of ordinary skill in the art with a reasonable expectation of success. *In re O'Farrell*, 853 F.2d 894, 7 U.S.P.Q.2d 1673 (Fed. Cir. 1988).

In considering a prior art reference, the reference must be considered in its entirety, *i.e.*, as a whole, including portions that would lead away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 U.S.P.Q. 303 (Fed. Cir. 1983), cert. denied, 469 U.S. 851 (1984). Moreover, it is improper to combine references where the references teach away from their combination. *In re Grasselli*, 713 F.2d 731, 743, 218 U.S.P.Q. 769, 779 (Fed. Cir. 1983).

B. Claims 6, 19, 20, 23 and 42 Are Patentable Over Kipshidze In View Of Coury

Regarding claims 6, 19, 20 and 42, the Examiner alleges that it would have been obvious to one of ordinary skill in the art to modify the composition of Kipshidze to include collagen, because Coury teaches that collagen activates or catalyzes the natural pathways of clotting (see Office Action, page 4, fifth to seventh paragraph). As to claim 23, the Examiner

alleges that it would have been obvious to one of ordinary skill in the art to modify the composition of Kipshidze to include protamine sulfate, because Coury teaches that protamine sulfate acts as an antidote to anticoagulation (see Office Action, page 4, last paragraph to page 5, second paragraph). In response, Applicants assert that claims 6, 19, 20, 23 and 42 are not obvious over Kipshidze in view of Coury to the extent that they depend from amended claim 2, which in turn is not obvious over these references for the following reasons.

As discussed above, Kipshidze discloses percutaneous administration of fibrin sealants to treat punctures in arterial and venous blood vessels, but does not teach or suggest topical administration over a catheter exit site on the skin of a patient, as recited in amended claim 2. In fact, Kipshidze does not teach or suggest any non-invasive means for applying its fibrin sealant. Instead, Kipshidze states that it is an object of its invention to provide an invasive method for applying a fibrin sealant, *i.e.*, directly to the external wall of an arterial or venous puncture site (see col. 2, lines 14-16), in order to form a seal or clot around the puncture which will prevent blood leakage from the vessel into the surrounding tissue (see col. 6, lines 22-26). Based on the teaching of Kipshidze, one of ordinary skill in the art would have no reason to expect that topical administration of Kipshidze's composition at a distance from the puncture in a femoral artery would be effective in treating such a puncture.

Coury does not cure the deficiencies of Kipshidze. Coury discloses a method of controlling hemostasis by applying a hemostatic agent in a tissue sealant composition, where the tissue sealant is a biodegradable, biocompatible synthetic polymer that may not intrinsically possess strong hemostatic properties (see Abstract). Like Kipshidze, Coury also does not teach or suggest applying its composition topically over a catheter exit site on the skin of a patient, as recited in amended claim 2. Therefore, the combination of Coury and Kipshidze does not teach or suggest all the limitations of amended claim 2.

Moreover, Applicants submit that one of ordinary skill in the art would have no reason to modify the composition of Kipshidze to include the additional elements disclosed in Coury, because Coury teaches away from using fibrin sealants such as those taught by Kipshidze. Specifically, Coury states that it is disadvantageous to use fibrin glues because they have little flexibility or extendibility once their deposition is complete (see col. 1, lines 24-26), and are unpredictable in terms of the time required for degradation and adherence to tissues (see col. 1, lines 26-30). By disparaging traditional fibrin glue compositions such as those taught by Kipshidze, Coury discourages the use of such compositions and offers no

reason for one of ordinary skill in the art to use the composition of Kipshidze, much less modify Kipshidze's composition to include the elements of the composition of Coury.

For at least the foregoing reasons, amended claim 2 and its dependent claims 6, 19, 20, 23 and 42 are patentable over Kipshidze in view of Coury. Withdrawal of the Section 103(a) rejection of claims 6, 19, 20, 23 and 42 is respectfully requested.

C. Claims 8-13, 16-18, 24 And 30 Are Patentable Over Kipshidze In View Of Cochrum

Regarding claims 8-13 and 18, the Examiner alleges that it would have been obvious to one of ordinary skill in the art to formulate the composition of Kipshidze as a solid, because Cochrum teaches the use of such compositions rapidly arrests bleeding and promotes rapid clot formation (see Office Action, page 5, fourth to sixth paragraphs). As to claims 16 and 17, the Examiner alleges that it would have been obvious to one of ordinary skill in the art to modify the composition of Kipshidze to apply it as a film or membrane because Cochrum teaches that the film or membrane is thinner and more flexible and therefore will have a decreased foreign body sensation (see Office Action, pages 5, second to last paragraph to page 6, first paragraph). As to claim 24, the Examiner alleges that it would have been obvious to one of ordinary skill in the art to employ the method of Kipshidze to the femoral artery because Cochrum teaches that the femoral artery is the largest artery which may result in rapid life-threatening blood loss if punctured and not immediately stabilized and Cochrum teaches a similar concept (see Office Action, page 6, second to fourth paragraphs). As to claim 30, the Examiner alleges that it would have been obvious to one of ordinary skill in the art to employ a compression bandage in combination with the composition of Kipshidze because Cochrum teaches the use of such induces rapid blood coagulation while maintaining constant and direct pressure on the site (see Office Action, page 6, fifth to seventh paragraph). In response, Applicants assert that claims 8-13, 16-18, 24 and 30 are not obvious over Kipshidze in view of Cochrum to the extent they depend from amended claim 2, which in turn is not obvious over these references for the following reasons.

As discussed above, Kipshidze does not teach or suggest a method for treating a puncture in a femoral artery resulting from a cardiac catheterization procedure in a patient by applying topically over a catheter exit site on the skin of a patient in need of such treatment a composition comprising an effective amount of one or more vasoconstrictor which does not comprise a poly-β-1→4N-acetylglucosamine polymer or derivative thereof, as recited in

amended claim 2. Cochrum does not cure the deficiencies of Kipshidze. Instead, Cochrum teaches the use of a syringe or forceps by way of which its composition can be applied directly to the puncture area of an artery or vein to plug the artery or vein (see page 16, paragraph [0229]; page 17, Example 5; and page 17-18, Example 8). Therefore, not only does Cochrum fail to provide the teaching or suggestion missing from Kipshidze, Cochrum also teaches away from topical administration, as recited in amended claim 2.

Moreover, Applicants submit that one of ordinary skill in the art would have no reason to modify the composition of Kipshidze to include the additional elements disclosed in Cochrum, because Cochrum teaches away from using fibrin sealants such as those taught by Kipshidze. Specifically, Cochrum states that the major problem connected with the use of fibrin sealants obtained from human donors, such as those taught by Kipshidze (see Kipshidze, col. 5, lines 4-13), is the threat of transmission of infectious diseases, such as AIDS and Hepatitis B and C (see Cochrum, page 3, paragraph [0039]). Moreover, Cochrum at page 3, paragraph [0038] warns against the risk of an immunogenic reaction to the fibrin glue, which is concentrated from human plasma by cryoprecipitation and precipitation, which are methods used by Kipshidze (see Kipshidze, col. 5, ll. 8-9). Furthermore, Cochrum describes other disadvantages of fibrin sealants, such as the necessity to keep each component of the sealant separate until the time of use, poor mechanical characteristics, difficulty of administration and undesirable adhesive characteristics (see page 4, paragraphs [0049] to [0051]). Thus, because Cochrum disparages the traditional fibrin glue compositions, such as those taught by Kipshidze, and teaches away from the use of such compositions, one of ordinary skill in the art would have no reason to modify the composition of Kipshidze to include the elements of the composition of Cochrum.

For at least the foregoing reasons, amended claim 2 and its dependent claims 8-13, 16-18, 24 and 30 are patentable over Kipshidze in view of Cochrum. Withdrawal of the Section 103(a) rejection of claims 8-13, 16-18, 24 and 30 is respectfully requested.

D. The Rejection of Claim 32 is Moot

The Examiner alleges that the method disclosed by Kipshidze is identical to that of claim 32 and therefore would result in the rate as claimed. Although Applicants disagree, solely to expedite prosecution of this application, claim 32 has been cancelled, thereby rendering the rejection of claim 32 moot.

CONCLUSION

Since all claim rejections are believed to be overcome, all claims are believed to be in condition for allowance. An early notice to that effect would be appreciated. Should the Examiner not agree with the Applicants' position, then a personal or telephonic interview is respectfully requested to discuss any remaining issues and expedite the eventual allowance of the application.

Applicants respectfully request that the above amendments and remarks be entered and made of record in the file history of the instant application.

Respectfully submitted,

Date: January 16, 2009

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